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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/534,988	05/16/2005	Lasse Leino	OHMAN-002	1914

32954 7590 10/02/2007

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EXAMINER	
SIMMONS, CHRIS E	

ART UNIT	PAPER NUMBER
1614	

MAIL DATE	DELIVERY MODE
10/02/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/534,988	LEINO ET AL.	
	Examiner	Art Unit	
	Chris E. Simmons	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16,17,19-22 and 28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16,17,19-22 and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the claims:

It is acknowledged that claims 16-17 and 19 are currently amended, claim 18 is cancelled, and claim 28 is added in the response filed on 12/20/2006.

Claims 16-17 and 19-22 and 28 are presented for examination.

Claim Rejections - 35 USC § 112 – 1st Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 16-17 and 19-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating topical inflammatory disorders comprising cis-urocanic acid, does not reasonably provide enablement for the prevention of disorders characterized by local inflammatory reaction curable by immunosuppression. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. This is Scope of Enablement rejection.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2nd 1400 at

1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The ability of preventing disorders characterized by local inflammatory reaction curable by immunosuppression is not yet known in the art. The burden of enabling one skilled in the art to prevent such disorders would be much greater than that of enabling the treatment of a representative number of diseases. In the instant case, the specification does not provide guidance as to how one skilled in the art would accomplish the objective of preventing disorders characterized by local inflammatory reaction curable by immunosuppression. Nor is there any guidance provided as to a specific protocol to be utilized in order to show the efficacy of the presently claimed active ingredients for preventing disorders characterized by local inflammatory reaction curable by immunosuppression.

No experimental evidence supporting the contention that the claim specified actives would actually prevent these diseases by simply administering the claim specified active agents has not been demonstrated nor practice the invention without an envisaged endpoint or result of the treatment (note the absence of such recitation in the current claim(s)). The specification fails to enable one of ordinary skill in the art to

practice the presently claimed method for preventing and for practicing same without a specific endpoint for the treatment of the claimed diseases.

The term "prevention" or "preventing" is synonymous with the term "curing" and both circumscribe methods of treatment having absolute success. Since absolute success is not as of yet reasonably possible with most diseases/disorders, especially those having etiologies and pathophysiological manifestations which are as complex/poorly understood as "disorders characterized by local inflammatory reaction curable by immunosuppression".

The amount of direction or guidance presented:

The specification does not provide any guidance in terms of preventing disorders characterized by local inflammatory reaction curable by immunosuppression.

The presence or absence of working examples:

No working examples are provided for preventing disorders characterized by local inflammatory reaction curable by immunosuppression, for example in a patient, in the specification. The applicant has not provided any competent evidence or disclosed any tests that are highly predictive for the preventative effects of the instant composition. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

The quantity of experimentation necessary:

The quantity of experimentation would be undue to one of skill in the art and amount to the trial and error type of experimentation without a priori expectation of success. Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims.

In view of the breadth of the claims, the chemical nature of the invention and unpredictability of preventing disorders characterized by local inflammatory reaction curable by immunosuppression, and the lack of working examples regarding the activity as claimed, one skilled in the art would have to undergo an undue amount of experimentation to use the instantly claimed invention commensurate in scope with the claims.

In consideration of each of factors 1-8, it is apparent that there is undue experimentation because of variability in prediction of outcome that is not addressed by the present application disclosure, examples, teaching and guidance presented. Absent factual data to the contrary, the amount and level of experimentation needed is undue.

Claims 16-22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to

one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a Written Description rejection.

The claims recite "a pharmaceutically acceptable agent" and "said agent" (e.g., claim 1, lines 6-7 and 9). There is insufficient written basis in the specification for a pharmaceutically acceptable agent other than cis-uracanic acid.

Regarding the requirement for adequate written description of chemical entities, Applicant's attention is directed to the MPEP §2163. In particular, *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1568 (Fed. Cir. 1997), *cert. denied*, 523 U.S. 1089, 118 S. Ct. 1548 (1998), holds that an adequate written description requires a precise definition, such as by structure, formula, chemical name, or physical properties, "not a mere wish or plain for obtaining the claimed chemical invention." *Eli Lilly*, 119 F.3d at 1566. The Federal Circuit has adopted the standard set forth in the Patent and Trademark Office ("PTO") Guidelines for Examination of Patent Applications under the 35 U.S.C. 112.I "Written Description" Requirement ("Guidelines"), 66 Fed. Reg. 1099 (Jan. 5,2001), which state that the written description requirement can be met by "showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics," including, *inter alia*, "functional characteristics when coupled with a known or disclosed correlation between function and structure ..." *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 296 F.3d 316, 1324-25 (Fed. Cir. 2002) (quoting *Guidelines*, 66 Fed. Reg. at 1106 (emphasis added)). Moreover, although *Eli Lilly* and *Enzo* were decided within the factual context of DNA sequences, this does not preclude extending the reasoning of those cases to chemical structures in

general. *Univ. of Rochester v G.D. Searle & Co.*, 249 Supp. 2d 216, 225 (W.D.N.Y. 2003).

Applicant has failed to provide any structural characteristics, chemical formula, name(s) or physical properties of a pharmaceutically acceptable agent, aside from a broad recitation that such are contemplated for use in the invention. As such, it is not apparent that Applicant was actually in possession of, and intended to be used within the context of the present invention, any pharmaceutically acceptable agent other than cis-urocanic acid at the time the present invention was made.

Claim Rejections - 35 USC § 112 – 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 16-17, 19-22, and 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 16 recites the limitation "essentially non-dissociated". The term "essentially" in claim 16 is a relative term, which renders the claim indefinite. The term "essentially" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Accordingly, it is unclear how much agent is in the non-dissociated form.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 16-17, 19-22 and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent 5,494,676 ('676).

'676 teaches the method of treating inflammatory diseases, including psoriasis, comprising administering a topical composition (column 1, line 15) comprising cis-urocanic acid (col 1, line 50-end). As for the limitation, "capable of acidifying cell cytoplasm", any agent is "**capable** of acidifying cell cytoplasm", especially an acid such as cis-urocanic acid. As for the pH range, the composition was prepared by buffering the urocanic acid solution to a pH of 6.9. Absent evidence to the contrary, it is reasonable to one of ordinary skill in the art that the final composition of Experiment 1 of the reference is near neutral (i.e., a pH of 6.9) and, therefore, it is highly reasonable to conclude that the weak acid, cis-urocanic acid, is essentially non-dissociated.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and

> the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 16-17, 19-22 are rejected under 35 USC 103(a) as being unpatentable over Ben-Basset et al. ("*Inhibitors of Tyrosine Kinases in the Treatment of Psoriasis*"; Current Pharmaceutical Design, 2000, Vol. 6 No. 9: 933-942).

Determination of the scope and content of the prior art (MPEP 2141.01)

Ben-Basset et al. discloses the treatment of psoriasis by administering tyrosine kinase inhibitors such as, AG 18 (p. 938 under Group II; page 939 column 2, second paragraph).

Ascertainment of the difference between the prior art and the claims (MPEP 2141.02)

Ben-Basset et al. does not disclose expressly the pH range from 6.1-7.0.

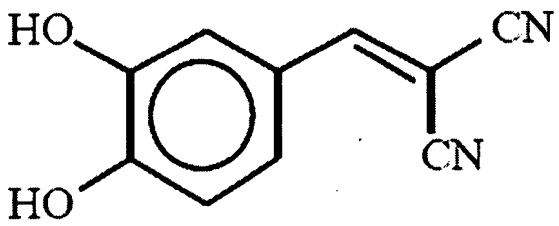
Finding of prima facie obviousness

At the time of the invention it would have been obvious to a person of ordinary skill in the art to treat psoriasis by administering a composition comprising an agent in essentially non-dissociated form.

As for the pH limitation, it is not patentable to optimize the pH range of a composition through routine experimentation. Differences in pH from what is disclosed in the reference, will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such pH is critical. It is not inventive to discover the optimum or workable ranges by routine experimentation. (See MPEP 2144.05 [R-5] II A).

As for the limitation that the agent is non-dissociated, it is reasonable to conclude that the compound having the structure of AG 18 is essentially non-dissociated when administered.

The structure of AG 18 is:



AG 18

Rational and Motivation (MPEP 2142-2143)

The suggestion/motivation for doing so would have been provide an optimal pH at which the agent would have the desired effect and outcome. Additionally, a pH near neutral would cause minimal irritation to the skin.

Therefore it would have been obvious to treat a disease characterized by local inflammatory reaction as claimed.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976). In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one

of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 16-22 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 13-18 and 20-23 of copending Application No. 11408056 in view Granstein Psoriasis (Further Evidence of a Key Role for Leukocytes. J. Clin. Invest. Volume 98, Number 8, October 1996, 1695-1696).

Although the conflicting claims are not identical, they are not patentably distinct from each other because the methods both comprise the topical administration of cis-urocanic acid for the treatment of psoriasis for example, which is characterized by a dramatic increase in epidermal proliferation (see Granstein).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 16-22 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 16-21 and 23-26 of copending Application No. 10565202 in view Granstein Psoriasis (Further Evidence of a Key Role for Leukocytes. J. Clin. Invest. Volume 98, Number 8, October 1996, 1695-1696).

Although the conflicting claims are not identical, they are not patentably distinct from each other because the methods both comprise the topical administration of cis-urocanic acid for the treatment of psoriasis for example, which is characterized by a dramatic increase in epidermal proliferation (see Granstein).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chris E. Simmons whose telephone number is (571) 272-9065. The examiner can normally be reached on Monday - Friday from 7:30 - 5:00 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Chris Simmons
Patent Examiner
AU 1614

September 20, 2007

ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER

DOA